PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PXWO00343/2004	**FOR FURTHER ACTION** See Form PCT/IPEA/416	
International application No. PCT/ES2004/000282	International filing date *(day/month/year)* 17.06.2004	Priority date *(day/month/year)* 04.07.2003
International Patent Classification (IPC) or national classification and IPC A61K9/51		
Applicant ADVANCED IN VITRO CELL TECHNOLOGIES, S.L. et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
31.03.2005	02.03.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Villa Riva, A Telephone No. +49 89 2399-8404

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/ES2004/000282

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-14 as originally filed

   Claims, Numbers

   1-15 as originally filed

   Drawings, Sheets

   1/7-7/7 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2,4,8,9,13
	No:	Claims	1,3,5-7,10-12,14,15
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-15
Industrial applicability (IA)	Yes:	Claims	1-15
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: LOURENCO C. ET AL.: 'Steric stabilization of nanoparticles: size and surface properties' INT. J. PHARMACEUTICS vol. 138, 1996, pages 1 - 12
D2: WO 96 20698 A2
D3: SANCHEZ A. ET AL.: 'Biodegradable micro- and nanoparticles as long-term delivery vehicles for interferon-alpha' EUR. J. PHARM. SCIENCES vol. 18, no. 3-4, March 2003, pages 221 - 229
D4: US-A-5 962 566

Unless otherwise indicated, reference is made to the relevant passages emphasized in the International Search Report.

The subject-matter of present claims 1,3,5-7,10-12,14,15 does not appear to be novel as required by Art. 33(1) and (2) PCT over D4. D4, col. 3, lines 17-29, or example 1 discloses the preparation of nanoparticles by obtaining a homogeneous mixture of a biocompatible polymer (e.g. PLGA), a so-called interacting agent like a poloxamer, a drug (e.g. somatotropin) in an organic solvent, removing the solvent and separating the particles. This is the same process as claimed in claim 1. Ratios and molecular weights also overlap. The use of the nanoparticles for the preparation of pharmaceutical compositions is contemplated as well.
A similar process is disclosed in D1, although the ratios are not disclosed, whereas in D3 rather an encapsulation process is disclosed.

Step e) (lyophilisation), the use of a polyanhydride instead of a polyester and the use of poloxamine instead of poloyxamer is not disclosed in the cited prior art. Hence the subject-matter of present claims 2,4,8,9,13 is formally novel.

As far as the lyophilisation is concerned, it is common practice in galenics, especially for degradable active principles like proteins. As far as the use of poloxamine and

polyanhydride is concerned, in fact, they appear to be just alternative solutions to the problem how to provide nanoparticulate carriers for drugs, without any inventive contribution. No examples are provided.

Hence the presence of an inventive step under Art. 33(1) and (3) PCT does not appear to be acknowledgeable to present claims 1-15 even in presence of novel embodiments in some claims.